

**REMARKS****Specification**

The specification has been amended to recite the full names of the references in lieu of the numbers as requested by the Examiner in the Office Action mailed March 13, 2003. Applicant submits that specific, direct and positive request to enter these amendments are presented in the instant reply.

**Rejections Under 35 USC §112, 1<sup>st</sup> Paragraph**

Claims 7 and 9-22 are rejected under 35 U.S.C. §112, first paragraph, for failing to comply with written description requirement. This rejection is respectfully traversed.

The Examiner contends that the as-filed specification does not describe a method of making miniarray with spots having center-to-center spacing of about 0.5 mm to about 3 mm. The Examiner contends that the as-filed specification teaches center-to-center spacing of about 1 mm to about 3 mm. Accordingly, Applicant has amended claim 1 to recite miniarray with spots having center-to-center spacing of about 1 mm to about 3 mm. Applicant submits that the subject matter of the amended claim is fully supported by the disclosure of the present specification. Hence, Applicant respectfully requests that the rejection of claims 7 and 9-22 under 35 U.S.C. §112, first paragraph, be withdrawn.

**Rejections Under 35 USC §103(a)**

Claims 7 and 9-22 are rejected under 35 USC §103(a) as being unpatentable over **Brown et al.** (U.S. Patent 5,807,522) in view of **Lange** (abstract) or over **Van Ness et al.** (U.S. Patent 6,248,521) in view of **Lange** (abstract). This rejection is respectfully traversed.

The present invention relates to a miniarray which is simpler and less expensive as compared to the sophisticated microarrays of the prior art of **Brown et al.** or **Van Ness et al.** The development of high density microarrays of the prior art comes at great cost and limitations, since the equipment required is complex and delicate, specialized temperature and humidity controls and enclosures are required, and complex robotic procedures must be programmed for each run. The uses of high-density microarrays requires dust free "clean room" conditions and equipment that parallel the specialized facilities required for the manufacture of computer chips. Such microarrays also requires the use of very expensive, specialized labeling reagents (instant specification, page 6, lines 7-16). In contrast, fabrication of the miniarray of the present invention requires less complex equipment, and is less sensitive to dust or humidity conditions. The miniarrays of the present invention can be analyzed with simpler method and machine, yet still provides high quality expression assays that exhibit diagnostic value comparable or equivalent to the more expensive, high-density microarray assays (page 10, lines 1-5, 11-17).

The miniarray of the present invention comprises assay spots that have a center-to-center spacing of about 1 mm to about 3 mm. In contrast, **Brown et al.** teach microarrays that have assay spots 10-250  $\mu$ m in diameter and separated from other assay spots in the array by about the same distance (column 6, lines 32-37). **Brown et al.** also teach a microarray having assay spots 20-200  $\mu$ m in diameter and a center-to-center spacing in the range of 20-400  $\mu$ m (column 9, lines 30-40).

The Examiner contends that since **Brown et al.** teach a center-to-center spacing of 400  $\mu$ m that approximates the instant invention of 0.5 mm, the claimed miniarray is *prima facie* obvious over the teaching of **Brown et al.** Applicant respectfully disagrees. Applicant submits that the present invention teaches a center-to-center spacing of 1-3 mm, which is at least more than double of 400  $\mu$ m taught in **Brown et al.** Hence, the teaching of **Brown et al.** does not approximate

the teaching of the present invention, and *prima facie* obviousness is not established in view of **Brown et al.**

The Examiner also contends it is *prima facie* obvious that center-to-center spacing is a result effective variable well within the realm of one having ordinary skill in the art. Applicant respectfully disagrees. Applicant submits that in order to establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations (M.P.E.P §2143). The teaching or suggestion to make the claimed invention must be found in the prior art, not in applicant's disclosure (M.P.E.P §2143).

**Brown et al.** is discussed above. The Examiner cites **Lange** (abstract) as a disclosure on the use of disposable pipette. Applicant submits that **Brown et al.** and **Lange** do not teach or suggest all the claim limitations of the present invention. **Brown et al.** and **Lange** do not teach or suggest modifying the microarray and increasing the center-to-center spacing up to 1-3 mm to change the microarray into miniarray as claimed herein. Absent any teaching or suggestion to change the microarray into miniarray as disclosed herein, it is irrelevant whether changing center-to-center spacing is within the realm of one having ordinary skill in the art. The case of *prima facie* obviousness simply fails in the absence of any motivation to change the microarray of **Brown et al.**

Indeed it is implausible to find in the disclosure of **Brown et al.** a motivation to change the invention of **Brown et al.** into miniarrays as disclosed herein. It is generally recognized in the art that microarrays such as those of **Brown et al.** are state of the art technology that provide high density and high throughput gene expression analysis. Neither **Brown et al.** nor the Examiner provides any teaching that suggests any limitation or drawback on the microarrays. Consequently, neither **Brown et al.** nor the Examiner provides any need or motivation to change the microarray of **Brown et al.**, let alone changing the microarray into a lower density and lower throughput format of miniarray as disclosed herein. In conclusion, Applicant submits that the present invention is not *prima facie* obvious over **Brown et al.** and **Lange** because the cited references neither provide a motivation to

change the invention nor teach or suggest all the claim limitations of the present invention.

With regard to **Van Ness et al.**, the Examiner contends that it basically teaches the same method as **Brown et al.** The Examiner further concludes that "Van Ness clearly teaches that CTC is a result effective variable that can be varied depending upon factors such as the desired diameter of the spots dispensed." Applicant respectfully disagrees.

Applicant submits that the Examiner's assertion is not supported by the disclosure of **Van Ness**. The passage cited by the Examiner (column 6, lines 54-60) merely describes general features of the microarray, e.g. spot size and distance between the spots. The cited passage does not teach or suggest any relationship between spot size and distance between the spots, let alone teach or suggest modifying the distance between the spots due to the size of the spots.

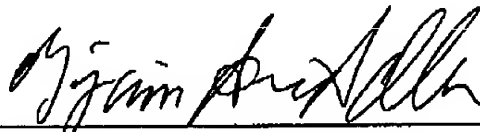
Since **Van Ness et al.** teaches the same as **Brown et al.**, the above argument with regard to **Brown et al.** is equally applicable here. Applicant submits that **Van Ness et al.** and **Lange** (abstract) do not teach or suggest all the claim limitations of the present invention. **Van Ness** and **Lange** do not teach or suggest modifying the microarray and increasing the center-to-center spacing up to 1-3 mm to change the microarray into miniarray as claimed herein. As discussed above, absent any teaching that provides motivation to change the high density microarray into a lower density miniarray of the present invention, the present invention is not *prima facie* obvious over **Van Ness et al.** and **Lange**.

In view of the above remarks, Applicant submits that the invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicant respectfully requests that the rejection of claims 7 and 9-22 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Final Office Action mailed November 6, 2003. If any issues remain, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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